Listing of Claims:

1. (Currently amended) A method for screening for an agent effective to inhibit the development of malignancies associated with a chronic viral infection, whereby said viral infection is caused by a virus which contains a viral protein with an interferon sensitivity determining region (ISDR), comprising:

incubating a mixture containing RNA-activated protein kinase (PKR), wherein PKR comprises a protein kinase catalytic domain of PKR, the viral protein, and an agent to be tested, and measuring PKR protein kinase activity, comparing to PKR protein kinase activity in the absence of the agent to be tested, and identifying a potential agent by the indication of PKR protein kinase activity in the presence of the agent.

2. (As Filed) The method of Claim 1 wherein the agent inhibits the malignancies associated with chronic hepatitis C viral infection.

3. (As Filed) The method of claim 1 wherein the viral protein is NS5A.

4. (Currently amended) A method of screening for an agent effective to inhibit the development of malignancies associated with a chronic viral infection, whereby said viral infection is caused by a virus which contains a viral protein with an interferon sensitivity determining region (ISDR), whereby said agent is effective in inhibiting the direct interaction of an ISDR containing viral protein with an interferon induced RNA-activated protein kinase (PKR), comprising:

incubating a mixture containing the ISDR containing protein, PKR, wherein PKR comprises the protein kinase catalytic domain of PKR, and an agent to be tested, and measuring the binding of the ISDR containing protein and PKR,

comparing to the degree of binding in the absence of the agent to be tested, and identifying a potential agent by the indication of PKR protein kinase activity in the presence of the agent.

5. (As Filed) The method of Claim 4 wherein the viral protein is NS5A.

6. (As Filed) The method of Claim 4 wherein the agent inhibits the malignancies associated with chronic hepatitis C viral infection.

7. (Previously Presented) The method of Claim 1, wherein PKR and the protein containing an ISDR are expressed in a yeast cell genetically engineered to increase expression of a reporter gene in the presence of activated PKR, and further comprising measuring the level of expression of the reporter gene in the presence and absence of the agent to be tested.

8. (As Filed) The method of Claim 7, wherein the reporter gene product is fused to GCN4/ -gal protein.

9. (Currently Amended) A method for screening for agents, the method comprising the step of contacting an agent with a yeast cell which is genetically engineered to express:

(a) a polypeptide containing an ISDR region, and

(b) an interferon-induced RNA-activated protein kinase (PKR), wherein PKR comprises a protein kinase catalytic domain of PKR, and

(c) a reporter gene whose expression is increased in response to activation of PKR, and further comprising the step of measuring the level of expression of the reporter gene in the presence and absence of the agent to be tested.

10. (As Filed) The method of Claim 9 wherein the polypeptide containing an ISDR region is NS5A.

11. (As Filed) The method of Claim 10 wherein the reporter gene is a fused GCN4/ - gal gene.

12. (Cancelled)

13. (Currently Amended) A method comprising:

a) incubating a reaction mixture comprising

i) a candidate agent;

ii) an NS5A polypeptide; and

iii) a RNA-activated protein kinase polypeptide (PKR), wherein PKR comprises a protein kinase catalytic domain of PKR; and

b) assaying for a difference in a property in the presence of said candidate agent as compared to said property in said reaction mixture incubated in the absence of said candidate agent,

wherein said difference in said property is indicative of the ability of said candidate agent to modulate the interaction of said NS5A polypeptide with said PKR polypeptide.

14. (Currently Amended) A method comprising:

a) providing a cell comprising a nucleic acid encoding an NS5A polypeptide and a nucleic acid encoding a RNA-activated protein kinase polypeptide (PKR), wherein PKR comprises a protein kinase catalytic domain of PKR, wherein said NS5A polypeptide and said PKR polypeptide can be expressed in said cell;

b) introducing into said cell a candidate agent; and

c) assaying for a difference in a property in the presence of said candidate agent as compared to said property in said reaction mixture incubated in the absence of said candidate agent in said cell,

wherein said difference in said property is indicative of the ability of said candidate agent to modulate the interaction of said NS5A polypeptide with said PKR-polypeptide in said cell.

15. (Previously Presented) The method according to claims 13 or 14, wherein said difference in said property is determined by assaying a decreased level in the binding of said NS5A polypeptide to said PKR polypeptide in the presence of said candidate agent, as compared to the level of binding of said NS5A polypeptide in the absence of said candidate agent, wherein said decreased level in the binding of said NS5A polypeptide to said PKR polypeptide in the presence of said candidate agent is indicative of the ability of said candidate agent to modulate the binding of said NS5A polypeptide to said PKR polypeptide.

16. (Previously Presented) The method according to claims 13 or 14, wherein said difference in said property is determined by assaying an increase in the level of dimerization of said PKR polypeptide in the presence of said candidate agent, as compared to the level of dimerization of said PKR polypeptide in the absence of said candidate agent, wherein said increase in the level of dimerization of said PKR polypeptide in the presence of said candidate agent is indicative of the ability of said candidate agent to modulate the interaction of said NS5A polypeptide with said PKR polypeptide.

17. (Previously Presented) The method according to claims 13 or 14, wherein said difference in said property is determined by assaying an increase in the level of phosphorylation of a substrate in the presence of said candidate agent as compared to the level of phosphorylation of said substrate in the absence of said candidate agent, wherein said increase in the level of said phosphorylation in the presence of said candidate agent is indicative of the ability of said candidate agent to modulate the interaction of said NS5A polypeptide with said PKR polypeptide.

18. (Previously Presented) The method according to any one of claims 13 or 14, wherein said NS5A polypeptide comprises a portion of the full length NS5A, wherein said portion contains the ISDR.

19. (Previously Presented) The method according to any one of claims 13 or 14, wherein said NS5A polypeptide comprises a portion of the full length NS5A, wherein said portion contains the PKR-binding domain of NS5A.

20. (Previously Presented) The method according to any one of claims 13 or 14, wherein said PKR polypeptide is induced by interferon.

21. (Cancelled)

22. (Previously Presented) The method according to any one of claims 13 or 14, wherein said PKR polypeptide comprises a portion of the full length PKR polypeptide, wherein said portion contains the NS5A-binding domain of said PKR polypeptide.

23. (Previously Presented) The method according to any one of claims 13 or 14, wherein said PKR polypeptide further comprises a portion of the full length PKR polypeptide, wherein said portion contains the dimerization domain of said PKR polypeptide.

24. (Previously Presented) The method according to any one of claims 13 or 14, wherein said PKR polypeptide comprises a portion of the full length PKR polypeptide, wherein said portion contains the catalytic domain of said PKR polypeptide.

25. (Previously Presented) The method according to any one of claims 13 or 14, wherein said candidate agent is a polypeptide that binds to said NS5A polypeptide.

26. (Previously Presented) The method according to any one of claims 13 or 14, wherein said candidate agent is an antibody that binds to said NS5A polypeptide.

27. (Previously Presented) The method according to claim 13 or 14, wherein said candidate agent is a nucleic acid that binds to the nucleic acid encoding said NS5A polypeptide.

28. (Previously Presented) The method according to claim 13 or 14, wherein said candidate agent is an antisense RNA or DNA, that binds to the nucleic acid encoding said NS5A polypeptide.

29. (Previously Presented) The method according to claim 13 or 14, wherein the expression of said PKR polypeptide is inducible.